

Cowl (W. Y.) Compliments of
the author
a

Is the Cause of Respiration the
Venosity of the Blood and
Tissue Fluid in the Re-
spiratory Center of the
Medulla Oblongata?

BY

W. Y. COWL, M. D.

REPRINTED FROM

The New York Medical Journal
for June 6, 1891.



*Reprinted from the New York Medical Journal
for June 6, 1891.*

IS THE CAUSE OF RESPIRATION

THE VENOSITY OF THE BLOOD AND TISSUE FLUID IN
THE RESPIRATORY CENTER OF THE MEDULLA OBLONGATA?

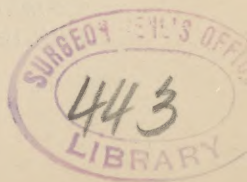
BY W. Y. COWL, M.D.

IN the issue of this Journal for November 22d last, in an article entitled *Some Remarks on my Hypothesis of the Self-regulation of the Respiration* and Dr. Cowl's Discussion of it, Dr. S. J. Meltzer asks my attention to the subject of the causation of respiration in the question hereafter following.

To this, by reason of the directness of the query, I desire briefly to respond, while at the same time expressing my satisfaction that he has not felt called upon to controvert the cogency of the facts I have adduced * to show the irrelevancy of the experimental results brought forward by him as a basis for his theory of the incitation of inspiration,† as well as the groundlessness of his criticism upon

* The Factors of the Respiratory Rhythm and the Regulation of Respiration. *N. Y. Med. Jour.*, Sept. 6, 1890.

† On the Self-regulation of Respiration. *Ibid.*, Jan. 18, 1890.



the existing theory of respiratory regulation, formulated and established by Gad.*

He asks, in general terms: "Does Dr. Cowl know of any experiment which shows that the blood, and that alone, is the exciting cause of respiration?"

For putting this question the author gives no grounds beyond a mere reference to my citation of a number of observers, who have shown the high sensitiveness of the respiratory center to changes in the constituents of the blood, and does not advert to those portions of my communication respecting the causation of respiration, or allude, except in two instances, to the published labors of the chief workers on this subject.

As, furthermore, he does not specify, on the one hand, whether he means simply the ordinary continuous respiration or also extraordinary respiratory efforts thereupon imposed, and, on the other hand, excludes from consideration the tissue fluids, which, from their constant renewal by the blood as well as because of the free diffusion of the gases dissolved therein to and from the vessels, are equally to be regarded (11), I can not assume to understand his meaning.

But, although this vagueness of his interrogation would call for explanation, I shall, rather than give rise to further disquisition, simply amplify in the required direction the basis of fact that I have previously given, and show the support which those facts are widely conceded to furnish for the essential causation of respiration by the excitants of the blood, by those substances, namely, which when increased in amount occasion increased respiration. This is of itself, at the present time, no ungrateful task, as the knowledge of the subject already established has, within

* Die Regulirung der normalen Athmung. Du Bois-Reymond's *Archiv*, 1880, p. 1.

the past few years, received a decided enrichment, which is not yet become common property.

In view of this enrichment, it may be said in advance, in respect of the known facts concerning the innervation of respiration altogether, that they solve, on the one hand, the problem of how it is that the first inspiration at birth comes to take place, and furnish, on the other, positive knowledge of the only means as yet demonstrated for the continuous incitation of respiration. By them, furthermore, the idea enunciated by Marshall Hall (1) that respiration was a reflex act wherein the incitation flowed to the respiratory center * from the brain, from the vagus, or from the sensory nerves in general, an idea which, notwithstanding a mass of experimentation directed toward its proof in these several respects, has at no time been shown to account in either of these ways for more than extraordinary respiratory efforts—*e. g.*, sighing, coughing, sneezing, anxious breathing—is now very definitely settled in the negative.

The theory of the peripheral origin of the incitation to respiration in general, of which Dr. Meltzer, in his former article, is the last exponent, would, by reason of its lack of support, have probably long since become disregarded were it not that it was broached in the first pretentious work upon this subject, and that it is a matter which is so apparent to the eye that the common extraordinary respiratory efforts result reflexly from sensorial impressions.

The first of the researches, which go to show that the incitation of inspiration is central and direct, and not peripheral and reflex, is that of Schwartz (2), entitled *Premature Respiratory Efforts; a Contribution to the Effect of*

* The commonly so denominated mechanism for the innervation of the respiratory efforts located in the medulla oblongata, and in general indispensable to respiration.

the Act of Birth upon the Fœtus, published in 1858, and noticed by Miescher (3) in the general article on the innervation of respiration contained in Du Bois-Reymond's *Archiv* for 1885 and cited in my previous communication. It is there stated that, "as the hinge upon which the existing view respecting the cause of the respiratory motions depends, the continually recurring question has been regarded, how, over against the quietude of uterine existence, does the first breath drawn come to take place? Is it the sensorial excitations of the act of birth, the cooling, the mechanical measures, by the fit application of which the halting respiration of the half-asphyxiated child is so beneficently aided, or does there lie something at bottom in the blood of the fœtus which is changed by the act of birth?"

"It is the same contradistinction which from the beginning until to-day permeates all discussions upon the respiratory movements, and, although the controversies are to-day more complicated than before, they are so, however, because various changes in the blood and various sensorial influences strive, as it were, for the governing place, or at least for a part of the territory.

"In view of so many apt statements of the older theories of respiration as exist, it will suffice for our object if we devote our discussion to the turning-point which the question of the origin of the first respiration passed by in the renowned work of Schwartz in 1858.

"Since Schwartz developed, more logically than had before been done, the idea that the premature respiratory movements of the fœtus, so feared in difficult labors, were always to be referred to some disturbance of the placental circulation—to cessation, therefore, of gaseous interchange between mother and child—this same mode of view has determined the conception of ordinary respiration, and this

has been clearly formulated and established in part through new researches by Rosenthal."

A second well-recognized work, by B. S. Schultze (4), which supports Schwartz's position, entitled *Apparent Lifelessness in the New-born*, is, like that of Schwartz, unfortunately, not at my command.

Within the past few years, however, two more complete experimental confirmations of the same idea have appeared. First, Zuntz and Cohnstein (5), in *Some Further Researches on the Physiology of the Mammalian Fœtus*, in treating of the causes of the normal apnoea* of the fœtus and of the first respiratory efforts of the new-born, record the following experiment upon the sheep, in which animal the placental tufts are so distributed about the walls of an unusually lax uterus that the opening of the latter and the extraction of the fœtus cause no interference necessarily with the placental circulation :

The research in question was made on February 2, 1885. At first only the tail and a fraction of the fore part of the trunk were exposed to the air.

Pinching, pricking, excitation of the pharynx and of the mucous membrane of the nose incited no inspiration.

Upon this, the animal was entirely extracted from the uterus and laid upon the abdomen of the mother, with careful avoidance of all traction upon the cord. Excitations now continued for several minutes, to which we added injection of air into the nose with a bellows, also produced no respiratory movement. The excitations mentioned induced numerous motor reflexes. The new-born animal sucked the finger and bit it when introduced deeper into the throat. Reflex motions did not regularly follow the excitations, but, on the other hand, there appeared frequent strong, spontaneous movements, which occasioned changes of position of the fœtus. The mucous membranes showed a normal red hue; no trace of cyanosis.

* Temporary absence of intermittent respiratory effort.

The first breath drawn followed almost immediately upon a ligation of the umbilical cord, and was succeeded by regular respiratory movements without any rattling. The fœtus continued to live. That it was full grown is proved by the weight of 2,860 grammes, the length of 48 centimetres, the development of the wool, and the energetic ingestion of nourishment.

It took at the first drink, about an hour after the tying of the cord, 60 grammes of milk.

We had therefore a normally apnœic fœtus under our hands, which was brought to breathe by no kind of excitation, but at once by cutting off the supply of oxygenated blood through the umbilical cord.

The authors note, in connection with this experiment, a source of deception which, in common with B. S. Schultze, they find in the usual means of inferring an absence of increase in the vensity of the blood actually furnished to the tissues of the fœtus (*i. e.*, mixed blood already considerably venous)—namely, by the brightness of color of the umbilical vein—for, as they very fully show, whenever the fœtal circulation is slowed, whether in the fœtus itself, as by an infrequency of the heart's action, or by compression of the umbilical vessels, the blood remains a longer time in the tufts of the placenta than otherwise, and therefore becomes more completely arterialized and of a brighter hue.

Thus, just when the blood in the umbilical vein, from its longer sojourn in the placenta, is more highly arterialized than normally, the tissues of the fœtus—its respiratory center therefore—are, nevertheless, suffering from a lack of arterial blood, a lack which affects both the quantity and quality of its supply; dyspnœa will, therefore, necessarily be developed, the same as by a slowing of the cerebral circulation in the grown animal (6).

O. Engström (7) has carried out in Preyer's laboratory a similar series of researches upon rabbits and guinea-pigs and in part by opening the uterus under warm salt water.

He finds, like the above-mentioned authors, that mechanical irritation of the fœtus alone will not induce respiration, but that stoppage or diminution of the placental circulation without such irritation will do so. He ascribes, nevertheless, to sensorial impressions a part in the excitation of the first breath drawn by the fœtus in general.

From the evidence, then, altogether, respecting the incitation of respiration at birth, we are justified in the statement that the essential cause of the first respiratory effort is the increased venosity of the blood supplied to the respiratory center of the fœtus.

That at many human births the fœtus does not respire until marked sensorial impressions be made upon it might, in view of the practice of delaying the ligation of the cord until respiration is established, be ascribed to a greater or lesser continuance of the placental respiration. How considerable, at any moment after normal birth, this latter respiration in general may be, we have as yet no accredited data for determining. Doubtless, whenever the uterus, freed from the bulk of the fœtus and the resistance to its birth, continues in contraction, the placental respiration must have ceased or have become much diminished, whereupon, by the direct resulting effect upon the respiratory center, and possibly also by the sense of cold to the surface, a respiratory effort, if nothing be there to hinder, will at once be induced. When, on the other hand, there are, after birth, intervals of non-contraction of the uterus, placental respiration may still continue and be sufficient for the needs of the fœtus.

The escape of blood of a markedly venous hue from the placental stump of the umbilical cord upon cutting it, after aerial respiration has begun, has evidently no certain bearing upon the question of persistence of placental circulation before this time, and may therefore be disregarded.

Those infrequent cases in which the cord is cut before respiration is established, chiefly in order to more effectively carry out measures of artificial respiration, are certainly in general, if not always, abnormal. A cause of halting respiration is obviously present, which is greater in its hindering effect than the increased venosity of the blood from the cessation of the placental functions, together with the peripheral excitations incident to birth, are in their incitatory action. This cause—the respiratory passages and other parts being normal—must be an abnormally diminished excitability of the respiratory center, and this may be explained by a previous prolonged diminution or cessation of the oxygen supply upon which the excitability of the center depends. A slight diminution in that supply in the fœtus must prevent respiration by allowing the excitability to sink below the point of effective excitation by the excitants offered to it by the blood and tissue fluid.

That the center normally possesses a markedly lesser degree of excitability in the fœtus than in the breathing animal has been rendered in the highest degree probable by Zuntz and Cohnstein (5); for, upon adding one per cent. of carbonic acid, as an excitant of increased respiration, to the respired air, at intervals for several days after birth, they found a continuous increase in the excitability of the center—an increase which they attribute to development of the same. As effective causes of such development of the center, there are the beginning of its function and the marked increase in the arterialization of the blood furnished to it upon the separation of the systemic and pulmonary circulations at birth; moreover, the blood of the umbilical vein itself can not necessarily be so well arterialized as the blood in the arteries of the self-respiring animal, which is shown, under normal circumstances, by the

fact that, as previously stated, the vein grows of a brighter red when compressed.

But this increased arterialization after aerial respiration is established coincides with increasing tissue activity generally; for Zuntz and Cohnstein (5) find that the differences between the respective amounts of carbonic acid on the one hand and of oxygen on the other in the blood of the umbilical vein and artery are, in each case, but about one half the difference between the same in the carotid artery and jugular vein, respectively, of the breathing animal. In estimating, furthermore, the actual consumption of oxygen by the tissues of the fœtus, a determination of the normal amounts of blood delivered to them in a unit of time enabled these observers to make a comparison between the fœtus and the grown animal, whereby it was found that the latter consumed about four times as much oxygen as the former. These observations showing a lesser consumption of blood in general before birth explain the low excitability of the fœtal respiratory center.

A diminution of the excitability of the respiratory center has been shown by Gad (6) to result, in the grown animal, from a diminished supply of arterial blood to that center. Similarly, upon the normally lower excitability of the respiratory center existing in the fœtus, a diminution may, furthermore, be imposed by conditions surrounding it for a time before birth attending the contraction of the uterus.

This contraction acts, first, by lessening the placental respiration through hindrance of the maternal placental circulation and through slowing of the circulation in the fœtus by slowing of its heart's action; secondly, in cases of head presentation, by directly diminishing the intracranial circulation. When the uterine contraction is quite persistent, as often occurs in these latter cases, the consequent diminution of excitability in the respiratory center may be

greater than the increase in the normal excitants of the blood resulting from the diminution of the placental respiration can compensate for; for, while the cranial pressure directly occasions an additional diminution of the excitability of the center, it does not, like the interference with the placental respiration, occasion corresponding increase of the respiratory excitants in the fœtal blood at large, but rather, indeed, by inhibiting muscular action, diminishes their production. Its direct influence remains, moreover, a superposed one when we take into account the fact that such pressure alone as found by Zuntz and Cohnstein will effect a slowing of the pulse and a slowing of the fœtal circulation, as evidenced by an increased brightness of color of the umbilical vein.

It is altogether, then, easy to perceive how, notwithstanding a ligation or section of the umbilical cord, a fœtus may not breathe. The greater frequency, moreover, of such a condition of non-respiration in a viable fœtus in man than in the lower animals coincides with the relatively larger size of the head in him. He has special need, therefore, of the accessory provisions for the incitation of the first inspiration furnished by nature, such as the response to the impression of cold or of flagellation. The action of these latter may evidently be either by reflex incitation of the center, or by increasing, more or less indirectly, through the general excitement, the excitability of the respiratory center to the normal direct excitants; in the former case they are immediately causative, in the latter evidently only conditional of respiration.

Cognizant of the extraordinary conditions at birth, that by exaggeration call at times for the marked action of the accessory provisions for the incitation of respiration in order to occasion the first inspiration; but, in view of the decisive fact that the hæmic excitants of respiration are

normally of themselves sufficient to occasion that effort, and that, despite the pulmonary arterialization of the blood, venous elements to a considerable amount still remain within it, we have the strongest possible presumption that the succeeding respirations—namely, the regular respiratory muscular action—are likewise incited through the venosity of the blood and tissue fluid contained within the respiratory center.

The further support for this position is contained in the proof of the great sensitiveness of the respiratory center in the more developed animal to changes in the constituents of the blood, and in a certain definite provision which has been shown to exist for the incitation of increased respiration, and to be directly due to increased tissue change within the organism (11).

Since the experiments of Traube, who held that the vagus was excited by the carbonic acid of the venous blood in the lungs (10), it has been known that the respiration of air containing this gas would evoke dyspnœa, and it has been shown in man by Miescher (3) that an addition of but one per cent. of this gas to the air respired results in a decided increase in the amount of air breathed, even without the knowledge of the subject of experiment. Traube's idea has gradually been given up, and it is now found by A. Loewy (8) that the same amount of increase in respiration on breathing air vitiated with carbonic acid occurs when in the animal the vagi are divided as when they are intact. From this it is most probable that such an increase of respiratory effort in man is not owing to excitation of the vagus by the venous blood or its carbonic acid in the lungs.

Very recent researches by Gad (9) concerning the deep inspirations which have been immediately induced by an inhalation of pure carbonic acid, or a strong admixture

thereof with air, show that this excitative action of carbonic acid is confined to the trachea and chief bronchi—parts not in contact with the venous blood laden with carbonic acid; and also that an atmosphere containing at least fifty per cent. of the gas is necessary to produce the reflex, a proportion greater than occurs even in the exhaled air from an almost asphyxiated animal. It is therefore clear that this excitant of respiration does not normally act by means of the vagus nerve. That, on the other hand, it does not first act upon the brain, and from thence reflexly upon the respiratory center of the medulla oblongata, but directly upon the latter, is rendered most probable by the observation of A. Loewy (8), that a like amount of increase of respiration upon adding a certain amount of carbonic acid to the respired air occurs before and after separating these nervous masses.

Thus Marshall Hall's first two alternatives are excluded; the third, that sensorial impressions occasion respiration, which was developed by Volkmann into the theory that the incitation to respiration lies simply in the excitation by carbonic acid of the sensory nerves in general, may be considered to be excluded, first, for respiration as a whole, by the experiment of Rosenthal (13), in which rhythmic respiration continued after all but a few of the sensory paths to the medulla oblongata were divided, an experiment that has since been repeated with greater completeness and the same result; and, secondly, for the proportionment of the amount of respiration to the needs of the organism, through the researches of Zuntz and Geppert (11). The latter found, by measuring the air respired, together with the amounts of oxygen consumed and of carbonic acid given off, by an animal under three different conditions—namely, of rest, of accustomed labor, and of muscular activity induced after section of the spinal cord above the origin of the

sciatic nerves by electrical excitation of these in their course—that, with the same increase of the respiratory interchange of oxygen and carbonic acid, denoting the same degree of muscular activity in the third as in the second case, the amounts of air respired were also the same, or nearly the same, in these latter cases.

Furthermore, upon cutting off the circulation in the active parts during the muscular excitation in the third case, the increase in respiration over that at rest failed to appear, and only did so when the vessels were let free, whereby the carbonic acid and other substances formed in the muscles during their activity came into the general circulation and thus reached the medulla oblongata.

Similar results have been obtained also by A. Loewy (8) in researches in which the brain was separated from the medulla oblongata, the spinal cord bisected in the mid-dorsal region, and the vagi divided.

It is evident from the foregoing, altogether, that the increased respiration during muscular activity was due to the venosity of the blood circulating in the respiratory center, and not to that in the tissues in general, nor to any sensorial impressions.

It is, moreover, plain from these experiments that a provision exists in the substances formed by muscular activity by which the amount of respiratory effort is directly governed at the respiratory center. That such a proportionment of the amount of air breathed to the need for it is in play, not only during pronounced muscular exertion, but also in that condition we denominate rest—a condition in which, when the skeletal muscular system is relatively quite relaxed, the main activities of the organism are the muscular contractions concerned in circulation, respiration, and the general production of heat (Fick, Pflüger)—is highly probable; is, indeed, tacitly assumed by Zuntz and Geppert.

But, if this is so, it affords a further support of the accepted view that the venosity of the blood and tissue fluid in contact or proximity with the substance of the respiratory center regulates the amount of respiration, which must then, in the existing absence of proof of other means of constant incitation of respiration, be considered to afford that continuous incitation altogether. We therefore consider it so, and might indeed refuse to entertain speculation as to whether sensorial impressions may in any way be concerned in this regulation, but a possibility seems nevertheless to exist that ordinary respiration is somewhat greater in amount than it otherwise would be by reason of a constant effect upon the respiratory center produced by sensorial impressions heightening its excitability to the normal direct excitants. This is, *a priori*, improbable, as the amount of respiration would then depend, not upon the needs of the organism as determined by tissue change, but upon the amount of nervous action present, which might or might not coincide therewith; again, supposing that efficient respiratory action was insufficient by reason of a failure of its help, it would add at least unnecessarily to the mechanism. But, beyond this, there is direct evidence to the contrary, namely, the observation by Loewy (12), that sleep both natural and artificially induced—*e. g.*, by chloral hydrate—does not alter the excitability of the respiratory center, while greatly reducing the amount of respiration through diminished formation of the normal direct excitants in the tissues in general.

That, in general, under extraordinary circumstances, the respiration may be increased by sensorial impressions needs no exemplification; but a continuance of such increase after the first breath or two is to be attributed to increased muscular or other activity induced by the same nervous impressions.

We are altogether, therefore, restricted to the venosity of the blood as the essential cause of the ordinary normal continuous respiration.

The one factor of this venosity which is positively known to be an excitant of the respiratory center is, as previously stated, carbonic acid. Of the others, a diminished alkalescence of the blood, occasioned by the formation of a more active acid than carbonic (lactic) in the muscles during their activity, is known (14) to diminish the receptivity of the blood for carbonic acid, thus effecting an increase of the latter in the tissues.

Lack of oxygen in the blood furnished to the medulla oblongata is in all probability never so great under normal circumstances as to give rise to excitation of the respiratory center; for a reduction in the amount of oxygen in a respired atmosphere to below 17 per cent. must take place before dyspnœa is developed, and before this point is reached there is already a reduction in the amount of oxygen consumed by the organism, as shown, respectively, in researches by Gad (15) and by Kempner (16).

In contradiction of the prevailing view of the central incitation of respiration, the only published researches are those of Marekwald (17), which are cited by Meltzer, together with an old experiment of Volkmann's, undertaken for another purpose, but lending itself to the arguments and cited by the first-named authors.

Marekwald's position is thus comparatively isolated. It has already received a very full reply, with experimental proof, to which I would refer (8). His main conclusion, thereby controverted, differs diametrically from those of Rosenthal, Pflüger, Gad, Zuntz, and numerous others in their researches. It is as follows: "The normal excitation of the respiratory center is not dependent on incitation upon the part of the blood, neither from deficiency of oxy-

gen nor from excess of carbonic acid in the blood," and is immediately followed by its support, to the effect that "animals without circulation and after exsanguification may continue to breathe for a long time."

Respecting this position and its supportive facts I would only note in particular that Marckwald and also Meltzer seem not to perceive that excitants of the respiratory center are necessarily still present in its tissue, being, under normal circumstances, only governed as to the amount there held by the amount of the same substances, or of other substances influencing their solubility, in the blood delivered to that center. Be there at any moment supposedly no carbonic acid within the tissue of the center, it must immediately diffuse thereto from the blood in the surrounding vessels. Be the blood, on the other hand, more or less drained from those vessels, as in the experiments of Volkmann and of Marckwald, or completely removed, as in some of the latter's researches, carbonic acid, nevertheless still remains in the center, and will continue to be produced there as long as substances are contained within the same, available to the generation of this product of tissue activity, and for just so long, probably, will the center continue to perform its function of inciting respiratory effort. In illustration and support of this explanation of the continuance of respiration in Marckwald's experiments, I would call especial attention to the latter portion of a remark concerning them that accompanies the description of one of the same, in which, after a removal of the blood in the vessels of the respiratory center by means of an injection of paraffin, the respiration still for a time continued. The observation is as follows: "I had frequent opportunity in animals bled to death (in the dog as well as the rabbit) to note the same [*i. e.*, respiratory effort], and chiefly when they had been bound for a long time." Now, it is ap-

parent from this that the respiratory function was at a minimum of activity, in which case, as is evident from our knowledge of the longer retention of functional power in the relatively less active respiratory center of the newborn than in that of the grown subject when deprived of air, the center would not so quickly lose its excitability on cutting off the blood supply as in the fresh animal, whereas the formation of carbonic acid there would be a diminished one, and therefore less quickly exhaust the center through the excitation offered by its progressively increasing amount.

Hence, so long as the center preserves a sufficient excitability after the cessation of the supply of fresh blood, so long will it continue to act. If the center has been ordinarily active, the stoppage of the blood-supply will be of quicker effect than when the animal be lethargic, hypnotized, or narcotized.

The same argument applies to Volkmann's experiment (18), which is of a similar character to those of Marckwald. The former is, however, interesting to us here, because of the object its author had in making it—namely, to show that respiration is not incited by means of the vagus or of the brain, as well as because of the particular fact developed and others contained in the description, which reads as follows: "I removed in a young cat the brain, with exception of the medulla oblongata; divided the vagus on both sides; and extirpated the lungs, with protection of the phrenic nerve. The breathing [efforts—C.] simply continued for forty minutes after the excerebration," and continues: "Had I not feared being influenced by theoretical considerations (later to be unfolded), I would say the inspirations increased, soon after the removal of the lungs, in force and frequency, Any way, the motions were very energetic; the diaphragm was strongly contracted; the

thorax strongly raised. I repeated the research on several young dogs with the same effect. At bottom these experiments unfold nothing unawaited, for it has long been known that an excised head continues to breathe [make nasal movements—C.] for some time (in young rabbits I have observed this seventeen minutes after the beheading).

“Thus one has occasion enough to believe that, without the accessory action of the vagus, an involuntary respiratory effort can take place.”

The striking thing about these passages to which I would call especial attention is the contribution they made and are held to have made to the improbability of the incitation of respiration through the vagus; indeed, it would seem as though Dr. Meltzer, by citation of this experiment, wished to express his present coincidence with its express teaching, for he makes no objection to Volkmann's immediate conclusion.

In explanation of the experimental result upon which his theory—if he still holds that theory—depends, Dr. Meltzer makes the statement that I ask for evidence that it was not due to dyspnœa from non-aeration of blood during the prolonged stoppage of respiration incident to his unusually strong excitations of the vagus.

To this I object, as I have asked of him nothing that was not published in his original communication.

I noted that he had not considered whether the inspiratory after-effect in question might be merely dyspnœa from vitiation of blood during the cessation of respiration. He now gives his reasons for his view. I believe, nevertheless, that this after-effect of his stimulations of the vagus was dyspnœic, and for the following reasons: First, any considerable simple cessation of respiration will produce dyspnœa as an after-effect; and, secondly, an expiratory

position of the chest—*i. e.*, a diminution in the volume of air still available within the pulmonary vesicles—will intensify such dyspnœa. But these conditions are essentially those of Dr. Meltzer's experiments. There is, however, a further similarity, and with reference to the vagus. In dyspnœa with unhindered respiratory passages, as upon marked muscular exertion, there must be, through the vagus, owing to the increased mean distention of the chest (6), an increased stimulation of the inhibitory nervous mechanism at the center, which is, however, overcompensated for by the increased excitants in the blood, due to the muscular exertion.

On the other hand, in a continuous stoppage of the respiration by an electrical excitation of the vagus, there is, first, an obviously increased stimulation of the inhibitory mechanism, above that in the normal respiration. The excitation hereby may be quite weak. When its amount, however, is increased far beyond such point of sufficiency, as in very strong electrical excitations of the vagus, the stimulation of the inhibitory mechanism will be correspondingly increased; for, as has been very fully shown by Bowditch, excitation of a nerve does not produce fatigue or exhaustion on its part. The full effect of the same, therefore, must come upon the center, and exhaustion or fatigue may be expected to appear in the manifestations of the latter; if not during such an excessive stimulation, at least upon its cessation.

Dr. Meltzer does not inform us to what degree or what constancy of expiration his excitations led; but he states that the effects are always expiratory when very strong currents are used, while they are uncertain with weaker ones. From this we may conclude that antagonistic factors were present in his electrical excitations of the vagus, which would therefore probably render impossible a measurement

of the effect of such excitation upon the inhibitory mechanism of the respiratory center.

That the effect upon the center, nevertheless, of strong excitation, particularly when prolonged, is itself strong may evidently be assumed; that it must be lasting is shown by the fact that the normal inhibition outlasts the excitation, as shown by Gad (6).

Secondly, during a stoppage of the respiration with contracted chest, the excitants of respiration in the blood rapidly increase.

So soon, then, in the case altogether, as the excessive excitation of the vagus is ceased, its stoppage plus the fatigue of the inhibitory mechanism will allow, and the increased excitants in the blood will therefore at once produce a very marked inspiratory after-effect.

The conclusion, therefore, appears justified that the inspiratory after-effect in Meltzer's experiments was dyspnoëic.

In conclusion, I would bring together a denial on his part of my understanding of his main position, with those portions of his previous communication from which I obtained that understanding. He now says: "Dr. Cowl further objects to the inference I am supposed to have drawn from my experiments on the trunk of the nerve [vagus—C.], that the lungs themselves are likewise provided with respiratory nerve fibers, and that these fibers exercise their function in ordinary breathing. On this point Dr. Cowl is mistaken; I did not draw any such conclusion from my experiments."

On pages 8, 10, 12, and 13 of his previous communication are the following paragraphs, in their order:

"On the other hand, it is equally certain that, at least in a number of individuals, medium strong and weak stimuli can positively produce inspiratory effects. Let us for the present keep in view the latter individuals. For these, then, we are

forced to assume that their vagi contain two kinds of fibers—those whose stimulation causes inspiration, and others whose stimulation inhibits inspiration.”

“But we can also conclude, wherever we find after an expiratory arrest an inspiratory after-effect, that inspiratory fibers are present in the trunk, and have been likewise stimulated in a latent manner.”

“But, as we have demonstrated in all animals under strong stimulation, such an inspiratory after-effect following an expiratory inhibition, we may conclude that both kinds of nerves exist in the vagus of all animals.”

“According to the view above set forth, I believe I am able to formulate a theory of respiration which is free from both objectionable features. In the first place, I assume that both fibers—those producing and those inhibiting inspiration—equally participate in the production of the rhythm.

“But I do not assume that both kinds of fibers are excited by particular specific stimuli. I simply mean to introduce the long after-effect of the inspiratory fibers as a factor in the mechanism. We have above made it plausible enough that during strong stimulation of the trunk of the vagus, or during expansion of the lung [!], both kinds of fibers are equally excited, and that in this the effect of the inhibitory nerves predominates; but that after cessation of the stimulation the long after-effect of the inspiratory nerve is manifested precisely as in the cardiac nerves. Thus I believe that normal [!] respiration, too, is effected according to the principle just explained.

“Inspiration expands the lung [!], thereby stimulating both the inspiratory and the inspiration-inhibiting nerve fibers.”

A comment upon these passages seems to me unnecessary. I would merely offer them as an excuse for not discussing his other remarks.

References.

1. Marshall Hall. *Memoirs on the Nervous System*. London, 1837.
2. Schwartz. *Die vorzeitige Athembewegungen*. Ein Bei-

trag zur Lehre von den Einwirkungen des Geburtsactes auf der Frucht. Leipsic, 1858.

3. Miescher-Rüsch. Zur Lehre der Athembewegungen. Du Bois Reymond's *Archiv*, 1885.

4. B. S. Schultze. *Der Scheintod Neugeborener.*

5. Cohnstein und Zuntz. Weitere Untersuchungen zur Physiologie des Säugethierfötus. Pflüger's *Archiv*, Band 42, 1888, p. 342.

6. Gad. Die Regulirung der normalen Athmung. Du Bois-Reymond's *Archiv*, 1880, p. 1.

7. Engström. Ueber die Ursache der ersten Athembewegungen. *Skandinavisches Archiv für Physiologie*, II, 2 and 3, p. 158; also *Centralblatt der Physiologie*, Dec. 6, 1890, Band 4, No. 18.

8. A. Loewy. Experimentelle Studien über das Athemcentrum in der Medulla Oblongata und die Bedingungen seiner Thätigkeit. Pflüger's *Archiv*, Band 42, 1888, p. 245.

9. Gad. Ueber Athemreflexe von den Hauptbronchen nach Versuchen des Herrn Zagari. *Verhandlungen der physiologischen Gesellschaft zu Berlin, 1889-'90.* Sitzung 25 Juli, 1890, No. 18; also in Du Bois-Reymond's *Archiv*, 1890.

10. Traube. *Gesammelte Beiträge*, Bd. i, S. 293.

11. Geppert und Zuntz. Ueber die Regulation der Athmung Pflüger's *Archiv*, Band 47, 1888.

12. A. Loewy. Zur Kenntniss der Erregbarkeit des Athemcentrums. Pflüger's *Archiv*, Band 47, 1888, p. 601.

13. Rosenthal. *Die Athembewegungen und ihre Beziehungen zum Nervus Vagus.* Berlin, 1862.

14. Lehmann. Ueber den Einfluss von Alkali und Säure auf die Erregung des Athemcentrums. Pflüger's *Archiv*, Band 42, 1888.

15. Gad. Ueber automatische und reflectorische Athemcentren. *Verh. der physiolog. Gesellschaft zu Berlin, 1885-'86.* May 5, 1886, Nos. 7 and 8; also Du Bois-Reymond's *Archiv*, 1886.

16. Kempner. Neue Versuche über den Einfluss des Sauerstoffgehaltes der Einathmungsluft auf den Ablauf der Oxyda-

tionsprocesse im thierischen Organismus. Du Bois-Reymond's *Archiv*, 1884.

17. Marckwald. Die Athembewegungen und deren Innervation beim Kaninchen. *Zeitschrift für Biologie*, 1886, p. 120.

18. Volkmann. Ueber die Bewegungen des Athems und Schluckens mit besonderer Berücksichtigung neurologischer Streitfragen. Müller's *Archiv für Physiologie*, 1841.



REASONS WHY

Physicians Should Subscribe

FOR

The New York Medical Journal,

EDITED BY FRANK P. FOSTER, M.D.,¹

Published by D. APPLETON & CO., 1, 3, & 5 Bond St.

1. **BECAUSE :** It is the *LEADING JOURNAL* of America, and contains more reading-matter than any other journal of its class.
2. **BECAUSE :** It is the exponent of the most advanced scientific medical thought.
3. **BECAUSE :** Its contributors are among the most learned medical men of this country.
4. **BECAUSE :** Its "Original Articles" are the results of scientific observation and research, and are of infinite practical value to the general practitioner.
5. **BECAUSE :** The "Reports on the Progress of Medicine," which are published from time to time, contain the most recent discoveries in the various departments of medicine, and are written by practitioners especially qualified for the purpose.
6. **BECAUSE :** The column devoted in each number to "Therapeutic Notes" contains a *résumé* of the practical application of the most recent therapeutic novelties.
7. **BECAUSE :** The Society Proceedings, of which each number contains one or more, are reports of the practical experience of prominent physicians who thus give to the profession the results of certain modes of treatment in given cases.
8. **BECAUSE :** The Editorial Columns are controlled only by the desire to promote the welfare, honor, and advancement of the science of medicine, as viewed from a standpoint looking to the best interests of the profession.
9. **BECAUSE :** Nothing is admitted to its columns that has not some bearing on medicine, or is not possessed of some practical value.
10. **BECAUSE :** It is published solely in the interests of medicine, and for the upholding of the elevated position occupied by the profession of America.

Subscription Price, \$5.00 per Annum. Volumes begin in January and July.

